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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/214,848	01/14/1999	TERUAKI SEKINE	SEKINE 1	8123

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EXAMINER	
CHOI, FRANK I	
ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/214,848	SEKINE, TERUAKI	
	Examiner	Art Unit	
	FRANK I. CHOI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,14,19-27,31,32,34 and 36-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,14,19-27,31,32,34 and 36-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 13,14,19-27,31,32,34,36-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ochoa et al. (US Pat. 5,296,353) in view of Babbit et al. (US Pat. 5,766,920), Ochoa et al. (U.S. Pat. 5,443,983), the acknowledged prior art, Wallace et al., Santamaria et al. and Sekine et al.

Ochoa et al. (US Pat. 5,296,353) teach activation of autologous T-lymphocytes with anti-CD3 (soluble or solid phase bound), such as OKT3, and cytokines, including IL-2, for treatment of cancers and diseases of viral etiology such as those caused by HIV, cytomegalovirus and Epstein Barr virus (See entire document, especially, Column 3, lines 32-50, Column 7, lines 54-68, Column 8, lines 1-35, Column 11, lines 29-54, Column 12, lines 15-54).

Babbitt et al. teach activation of autologous T-lymphocytes (including that taken from peripheral blood of virally infected patients) with OKT3 and cytokines, including IL-2, for treatment of tumors or viral pathogens, including herpesvirus (herpes simplex virus and cytomegalovirus), Epstein Barr virus and HIV (See entire document, especially, Column 2, lines 22-68, Column 3, Column 7, lines 40-49, Column 20, lines 53-68, Column 21, lines 1-16). It is disclosed that solid phase OKT3 may be used but that soluble OKT3 is preferred (Column 12, lines 1, 2).

Ochoa et al. (U.S. Pat. 5,443,983) teach a method of developing LAK activity in lymphocytes comprising contacting lymphocytes with IL-2 and an anti-CD3 antibody and a method of administering the same suspended in a phosphate buffered saline supplemented with human serum albumin to an AIDS patient (Column 11, lines 49-68, Column 12, lines 1-50, Claims 1-8).

Applicant acknowledges that T-cells are involved in cellular immunity against cancer and viruses (Specification, Pgs. 1, 2). Further, it is acknowledged that lymphocytes, including T-cells and NK cells, can be activated and stimulated by IL-2 and that lymphocytes can be activated and stimulated with IL-2, with or without CD3 antibodies, including against viruses, such as, EBV and CMV (Specification, pgs. 3,4).

Wallace et al. disclose activation of T-cell precursors from the circulation of seropositive individuals with IL-2 and that the same are effective against autologous EBV transformed cells (Page 1012, Abstract).

Santamaria et al. disclose cytomegalovirus primed peripheral blood mononuclear cells from seropositive subjects which are stimulated by anti-CD3 coated onto polystyrene beads plus interleukin-2 and that polystyrene coated with antibodies can induce the long term-growth of antigen specific T-cell lines in the absence of specific antigen and feeder cells (Page 1, Abstract, Pages 4-7).

Sekine et al. discloses that cultivation of T lymphocytes from peripheral blood lymphocytes with immobilized anti-CD3 (OKT3) and IL-2 induces a rapid proliferative response and that the immobilized form of anti-CD3 proved better for expansion than soluble anti-CD3 (Page 73, Summary, Page 74, Page 77, Discussion).

The prior art discloses compositions, methods of preparing and methods of using activated autologous lymphocytes which are derived from virally infected patients and activated and proliferated by the combination of anti-CD3 antibodies in soluble or solid phase and interleukin –2, where the viral infection can be HIV, cytomegalovirus and Epstein Barr virus. The difference between the prior art and the claimed invention is that the prior art does not expressly disclose excluding cytomegalovirus-infected patients or the use of anti-CD3 in solid phase. However, the prior art amply suggests the same as the prior art discloses the activation of autologous lymphocytes which can be used to treat viral infections, including viral infections other than cytomegalovirus, such as herpes simplex and Epstein Barr virus, which lymphocytes are activated by interleukin-2 and anti-CD3; that the use of solid phase anti-CD3 results in better proliferation than soluble anti-CD3; and the suspension of lymphocytes activated with interleukin-2 and anti-CD3 which are suspended in phosphate buffered saline and albumin. As such, it would have been well within the skill of one of ordinary skill in the art to prepare activated autologous T-lymphocytes from patients having viral infections other than cytomegalovirus, with the expectation that the activated autologous T-lymphocytes would be effective against said viral infections. Further, it would have been well within the skill of one or ordinary skill in the art to use solid phase anti-CD3 rather than soluble anti-CD3 with the expectation that suitable numbers of activated lymphocytes could be obtained at a faster rate. Finally, it would have been well within the skill of one of ordinary skill in the art to administer the activate autologous lymphocytes in a carrier containing phosphate buffered saline and albumin with the expectation that the same would be a suitable carrier.

The Applicant's arguments have been duly considered but they are deemed unpersuasive for the reasons of record, including that set forth in the Final Office Action (6/16/2006) and the

Advisory Action (5/21/2007) (said advisory action was in response to the latest amendment and reply of 2/15/2007 and responded to the arguments of the Applicant set forth therein).

The applicant cites to Glickstein et al., however, said reference was not cited in the rejection. As such, the Applicant has not shown that the prior art used in the rejection teaches away from the use of solid phase anti-CD3 antibodies. Further, the reference simply indicates that there was an increase in apoptotic cells in solid phase anti-CD3 versus soluble phase anti-CD3. There is no indication from the reference that would preclude the use of solid phase anti-CD3. A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994) (Claims were directed to an epoxy resin based printed circuit material. A prior art reference disclosed a polyester-imide resin based printed circuit material, and taught that although epoxy resin based materials have acceptable stability and some degree of flexibility, they are inferior to polyester-imide resin based materials. The court held the claims would have been obvious over the prior art because the reference taught epoxy resin based material was useful for applicant's purpose, applicant did not distinguish the claimed epoxy from the prior art epoxy, and applicant asserted no discovery beyond what was known to the art.).

The Applicant provides not evidence why one of ordinary skill in the art would be have a strong disincentive from combining Santamaria and Ochoa '353. The claims do not exclude specific antigen stimulation. Similarly with Wallace, the claims do not exclude antigen specific lymphocytes. The fact that HIV treatment was found by the inventor's to be ineffective is not material as the claims do not require treatment of HIV. Further, the fact that treatment of HIV was ineffective is insufficient to support a conclusion that treatment of EBV would be

ineffective. Obviousness does not require absolute predictability. The unsupported argument that in vitro activity may not reflect in vivo activity against EBV is not sufficient to overcome the rejection. The Applicant argues that the etiology of cancer differs significantly from viral infection, however, the prior art, as evidence by Ochoa et al., shows that the technique for proliferation of T lymphocytes is the same or similar. As such, the Applicant has not shown that difference in etiology would lead one from ordinary skill in the art away from the technique used in Sekine. With respect to Santamaria, the Applicant has provided no evidence that those skilled in the art would reasonably expect success mainly with the preferable cultivation time. In any case, since the Applicant had not shown that shorter cultivation times would be unsuccessful, the Applicant's unsupported argument is not sufficient to overcome the rejection. The Applicant provides not evidence that one of ordinary skill in the art would recognize that the risk of propagation of virus by taking lymphocytes from the blood of virally infected patient is high or that even if recognized that the same would preclude one of ordinary skill in the art from the technique disclosed and/or suggested by the prior art. The Applicant cites to no passage in Wallace that the authors of Wallace recognized the hypothetical risk of propagation of virus. The Applicant is reading facts into a reference which are not there. The same applies to Ochoa '983 and Santamaria, the Applicant cannot insert a hypothetical concern or risk that reference author's themselves did not specifically set forth. The prior art suggests the use of autologous T-lymphocytes from virally infected patients and the mere fact that the prior art did not have in vivo working examples of the same is not sufficient to overcome the rejection.

Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention has been collectively taught by the combined teachings of the references.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a compressed schedule and may be reached Monday, Tuesday, Thursday, Friday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frank Choi
Patent Examiner
Technology Center 1600
March 18, 2008

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616